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| 09/966,264 | 09/28/2001 | Elizabeth K. Barber | 896034605001 | 4008 |

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|---|---|
| KAUSHAL, SUMESH | |
| ART UNIT | PAPER NUMBER |
| 1636 | |

DATE MAILED: 05/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/966,264 | BARBER, ELIZABETH K. | |
| | Examiner | Art Unit | |
| | Sumesh Kaushal Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *15,19-21,24-36 and 39-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-18,22,23,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/05/03, 12/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## *DETAILED ACTION*

*Applicant's response filed on 03/22/04 has been acknowledged.*
*Claims 1-40 are pending and are examined in this office action.*
*Claims 15, 19-21, 24-36 and 39-40 are withdrawn from further consideration.*
*Claims 1-14, 16-18, 22-23 and 37-38 are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised **37 CFR §1.121**. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

## *Election/Restrictions*

1. Applicant's election with traverse of Group-I claims 1-14, 16-18, 22-23 and 37-38 in Paper No. 03/22/04 is acknowledged. The traversal is on the ground(s) that invention of group I (DNA) and II (antisense RNA) are capable of use together. The applicant further argues that the polynucleotides in invention I are required to produce the polypeptide sequences described in invention III (protein), from which the peptide recognition sequences of the antibodies in invention IV (antibodies) were derived. The applicant argues that the inventions I, II, III and IV are disclosed as capable of use together. The applicant further argues that the original claims were worded with the intent that the polynucleotides of group I would necessarily be required for the invention of group VI (diagnostic method). The applicant further argues that while the inventions could be distinct and separate, invention VI requires inventions I and IV.

This is not found persuasive because nucleic acid molecules, antisense RNA molecules, proteins, and antibodies are structurally and functionally distinct product which have different modes of operations functions and effects (see (MPEP 806.04, MPEP 808.01). For example, proteins and antibodies are biologically active compounds wherein the nucleic acids require an expression vector to express the encoded product. Furthermore an antisense RNA molecule is distinct form a nucleic acid sequence, since

the antisense RNA does not encode a protein but inhibits protein translation. Thus the inventions of groups I, II, III and IV are distinct and are of separate uses. In addition even though the nucleic acid sequences of invention I are required for a method for invention VI these inventions are distinct are of separate uses, since the nucleic acid sequences could also be used to make recombinant proteins or for method for gene therapy. The MPEP clearly states that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). Thus these inventions are distinct and are of separate use.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15, 19-21, 24-36 and 39-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 03/22/04.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-14, 16-18, 22-23 and 37-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of the instant invention encompasses a substantial functional equivalent of the polynucleotides (as claimed), wherein the polynucleotides comprising the DNA sequence of SEQ ID NO:1 and 10 to 150 additional consecutive nucleotides immediately upstream from SEQ ID N0: 1, wherein the polynucleotide is contained in SEQ ID N0: 2. The scope of invention as claimed further encompasses the nucleotide sequence of claim 1, wherein the DNA sequence of SEQ ID NO: 1 and the additional upstream nucleotides, or the substantial functional equivalent thereof comprise a region of DNA that is homologous to or identical to a region of DNA comprising a portion of the human dystrophin gene, wherein the DNA sequence of SEQ ID NO: 1, or its substantial functional equivalent, is inverted when compared to the same sequence of the human dystrophin DNA. In addition the scope of the polynucleotides as claimed encompasses a polynucleotides that encodes a polypeptide that binds to human CD33 protein. The scope of invention as claimed encompasses vectors and host cells comprising a substantial functional equivalent of SEQ ID NO:1. The scope of invention as claimed further encompasses any regulatory DNA element comprising a substantial functional equivalent of SEQ ID NO: or SEQ ID NO:2.

At best the specification discloses only one variant of the polynucleotide as claimed, which comprises polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1. The scope of invention as claimed encompasses addition of any 10-150 consecutive nucleotides, which would result in the variation of about 1-15% in the in the nucleotide sequences of SEQ ID NO:2. In addition the scope of invention as claimed encompasses a polynucleotide sequence comprising a functional equivalent of SEQ ID NO:2 which contains a functional equivalent of SEQ ID NO:1 (see claim 22). The specification fails to disclose any variant of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 or variant thereof explicitly or implicitly, wherein the variant is a functional variant of human dystrophin gene and is capable of binding to the human CD33 protein.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to

describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only teaches polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 but fails to disclose any variant of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1 or a variant of SEQID NO:1 that has the functional property of a human dystrophin-like gene product and/or binds to CD33 explicitly or implicitly as putatively claimed by the applicant.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses functional activity of dystrophin-like gene and/or binding to the human CD33 protein or any regulatory DNA element-like activity (i.e. promotor, binding site for any transcriptional factor), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics.

Furthermore the variation as claimed (1-15%) would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted added or deleted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

3. Claims 1-14, 16-18 22-23 and 37-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human Apo-dystrophin-4 gene which comprises the nucleotide sequence of SEQ ID NO:2 that contains the nucleotide sequences of SEQ ID NO:1, does not reasonably provide enablement for a polynucleotides encoding any other variant of Apo-dystrophin-4 gene, wherein the Apo-dystrophin-4 gene comprises any and all functional equivalent of the polynucleotides (as claimed). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

**Nature of Invention:**

The instant invention is drawn to a variant of human dystrophin gene designated herein as Apo-dystrophin-4.

**Breadth of Claims and Guidance Provided in the Specification**

The scope of the invention as claimed encompasses a polypeptide encoding a variant of human dystrophin gene comprising the DNA sequence of SEQ ID NO:1 and 10 to 150 additional consecutive nucleotides immediately upstream from SEQ ID NO:1 or a substantial functional equivalent of the human dystrophin gene, wherein the polynucleotide is contained in SEQ ID NO:2. The scope of invention as claimed further encompasses the nucleotide sequence of claim 1, wherein the DNA sequence of SEQ ID NO: 1 and the additional upstream nucleotides (as claimed), or the substantial functional equivalent thereof comprise a region of DNA that is homologous to or identical to a region of DNA comprising a portion of the human dystrophin gene, wherein the DNA sequence of SEQ ID NO:1, or its substantial functional equivalent, is inverted when compared to the same sequence of the human dystrophin DNA. In addition the scope of the polynucleotides as claimed encompasses a polynucleotides that encodes a polypeptide that binds to human CD33 protein. The scope of invention as claimed encompasses vectors and host cells comprising a substantial functional equivalent of SEQ ID NO:1. The scope of invention as claimed further encompasses a regulatory DNA element consisting of a substantial functional equivalent of SEQ ID NO:1 or SEQ ID NO:2.

At best the specification discloses only a single variant of Apo-dystrophin-4 gene sequence, which comprises polynucleotides of SEQ ID NO:2 containing the polynucleotides of SEQ ID NO:1. The specification discloses that the SEQ ID NO:1 is a 137bp long inversion sequence which begins at base pair location 860 and ends at base pair location 996 of the nucleotide sequences of SEQ ID NO:2 (996 bp) see Spec. page 3, para.1 fig-1). The specification further discloses that the nucleic acid sequence of SEQ ID NO:2 encodes a polypeptide which binds to human CD33 protein with low affinity.

**State of Art and Predictability**

The state of the art at the time of filing regarding dystrophin gene was such that the dystrophin gene is alternatively spliced throughout its coding sequence. Dystrophin is the largest known human gene. It extends over 3000 kb on the X chromosome and is transcribed into a 14-kb mRNA. The gene is composed of 79 exons that together

account for only 0.6% of the sequence. Its main protein product, dystrophin, a member of the spectrin superfamily, is a rod-shaped 427-kDa protein. Three full-length dystrophin isoforms have been described, each controlled by a tissue-specific promoter. The muscle isoform is mainly expressed in skeletal muscle but also in smooth and cardiac muscles; brain dystrophin is specific for cortical neurons but can also be detected in heart and cerebellar neurons, while the Purkinje-cell type accounts for nearly all cerebellar dystrophin. Furthermore alternative splicing provides a means for dystrophin diversification. The 3' region of the gene undergoes alternative splicing resulting in tissue-specific transcripts in brain neurons, cardiac Purkinje fibres, and smooth muscle cells while 12 patterns of alternative splicing have been described in the 5' region of the gene in skeletal muscle (Sironi et al, FEBS Lett. 517:163-166, 2002, see page 163, col.1). Furthermore the alternative splicing events are differentially regulated in different organs and that deletions involving the same exons can determine diverse splicing behaviours in different patients or even in different tissues of the same individual. In this view, allelic differences and tissue specificity in splicing factors should be regarded as possible determinants of disease expression and differential organ involvement (Sironi, page 166 col.2).

The myeloid restricted membrane glycoprotein CD33 is a member of the sialic acid-binding immunoglobulin-related lectin family, which mediates sialic acid-dependent cell interactions as a recombinant protein. The tyrosine phosphorylation of CD33 in myeloid cell lines is stimulated by cell surface cross-linking or by pervanadate, and inhibited by PP2, a specific inhibitor of Src family tyrosine kinases. The phosphorylated CD33 recruits both the protein-tyrosine phosphatases, SHP-1 and SHP-2, which modulate downstream signaling events associated with cell activation. The CD33 phosphorylation could be induced by ligand occupancy and subsequent clustering, which then trigger downstream signaling events in myeloid cells. Therefore the identification of CD33 ligand(s) is considered an important step in modulation of myeloid cell function via CD33 interaction especially in the treatment of acute myeloid leukemia (Taylor et al. J Biol Chem, 274(17):11505-11512, 1999, see abstract and page 11511 col.2 para.1) .

In the instant case the specification discloses that the SEQ ID NO:1 is a 137bp long inversion sequence which begins at base pair 860 and ends at base pair 996 of the nucleotide sequences of SEQ ID NO:2 (996 bp), see Spec. page 3, para.1 fig-1, fig-7). The scope of invention as claimed encompasses addition of any 10-150 consecutive nucleotides, which would result in the variation of about 1-15% in the in the nucleotide sequences of SEQ ID NO:2. Any variation as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976).

In instant case the specification fails to disclose any other variant of SEQ ID NO:1 or SEQ ID NO:2 explicitly or implicitly that is a substantial functional variant of human dystrophin gene and is also capable of binding to human CD33 protein which is consider the hallmark of acute myeloid leukemia. In addition the specification fails to disclose that polynucleotides of SEQ ID NO:1 encodes a protein or a polypeptide that is expressed on cell surface is vivo and is capable of binding to the human CD33 protein. Therefore considering the nature of dystrophin gene, which is known to be alternatively spliced, and complexities found in the modulation of CD33 mediated signal transduction by ligand binding, it is highly unpredictable that a substantial functional variants of the Apo-dystrophin-4 (as claimed) would bind to the human CD33 and/or have dystrophin gene like activity. Thus it would require an undue amount of experimentation to characterize every possible variant for the claimed functional activity (i.e. binding to CD33 and modulation of CD33 mediated signal transduction or as another splice variants of dystrophin gene which is express in tissue specific manner).

In addition the scope of regulatory DNA element as claimed encompasses a DNA sequence encoding a promoter, which regulates the transcription of a gene. The scope of regulatory DNA element as claimed encompasses a DNA sequence encoding any DNA binding site for a transcriptional factor, which regulates the gene expression to which it is linked. Besides the presence of a start codon and a stop codon the specification as filed fails to disclose and that polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 contains a promoter or any transcriptional factor binding sites which is capable of regulating the expression of a gene or other DNA sequences to which it is operatively linked. The specification fails to provide a single working example which establishes that polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 are capable of regulating the expression of a gene or a DNA sequence to which it is operatively linked. Therefore considering the limited amount of disclosure one would have to engage in undue amount of experimentation to explore whether the polynucleotides of SEQ ID NO:1 or SEQ ID NO:2 contains a promoter or any transcriptional factor binding site sequences which is capable of regulating the expression of a polynucleotide sequence of interest.

Regarding claims 17-18 the scope of the invention as claimed encompass a cell in-vivo, which contains the claimed nucleic acid sequences. Therefore, the invention reads upon a cell created by a method of gene therapy or making transgenic animal. The art at the time of filing clearly teaches that the gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations (Rosenberg et al, Science 287:1751, 2000). It has been difficult to predict the efficiency and out come of transduced genes because various factors govern the expression and/or therapeutic potential of transduced genes in vivo. The transduction of target cells represents the first critical step in gene therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacles to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets. Similarly, the state of transgenic art at the time of filing was such that phenotype of an

animal is determined by a complex interaction of genetics and environment. (Wood. Comp. Med. 50(1): 12-15, 2000, see page12). Therefore, considering the unpredictability in the art and the limited amount of guidance provided in the instant specification, it would require an undue amount of experimentation to exercise the invention as claimed. In instant case making a host cell to produce recombinant protein (in-vivo), wherein the host cells is created by method of gene therapy or transgenic art are not considered routine in the art and without sufficient guidance the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Claims 17-18 drawn to an isolated host cell would obviate this rejection.

Regarding claims 37 and 38 the scope of invention as claimed encompasses a pharmaceutical composition comprising polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:1, or functional variants thereof for the treatment of a disorder in which protein truncation plays a part. At best the specification teaches that CD33 is a cell surface marker used to differentiate between acute lymphocytic and acute myelocytic leukemias. On the other hand the specification teaches that the regulation of CD33 including those elements to which it binds in vivo, is not fully understood and there is a need for investigation of this biological system (spec. page 1, lines 17-20). The specification teaches that apo-dystrophin-4 is a putative low-affinity ligand for CD33. The specification teaches that given the association of CD33 with leukemia, the invention provides a means to inactivate expression of a gene correlated with a disease phenotype (spec page 23, lines 1-6). However considering the unpredictability found in the treatment of leukemia the specification fails to disclose a single working example which establishes that the administration of a polynucleotide sequence comprising the polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:1, or any functional variants thereof would lead to the treatment of acute myelocytic leukemia. For example the specification even fails to disclose that low-affinity binding of apo-dystrophin-4 to CD33 is capable of modulating CD33 mediated signal transduction in the proliferation myeloid leukemic cells (see Taylor et al. J Biol Chem, 274(17):11505-11512, 1999). In addition the specification fails to disclose any other disease or disorder in which truncation of

any protein play a part, wherein the disease is treatable by the administration of polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:1, or functional variants thereof. Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Thus considering the applicant's disclosure the pharmaceutical composition comprising the claimed polynucleotide sequences is not found enabled for the treatment of any disease or disorder.

In addition screening of any and all natural and/or non-natural variants of Apo-dystrophin-4 gene product, wherein unknown numbers of amino acid sequences are added substituted and/or deleted is not considered routine in the art. Making and testing a point mutation is significantly different from the making and testing a gene product wherein unknown amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed functional activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The applicant has not presented enablement commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-14, 16-18 22-23 and 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and 22 are indefinite because it is unclear how "a substantial functional equivalent of the polypeptide" (as claimed) could be contained in the polynucleotides sequences of SEQ ID NO:2. The SEQ ID NO:2 is nucleotide formula which has a predefined nucleotide sequence and contains the nucleotide sequences of SEQ ID NO:1. According to the instant specification the substantial functional equivalents of polynucleotides of the invention include all mutants or variants that differ by base pair additions, deletions, substitutions or inversions, or other mutations (spec page 18 lines 16-20). Therefore nucleotide sequences of any functional equivalent as claimed would certainly differs form the nucleotide sequences contained in the SEQ ID NO:2. Thus it is unclear how the polynucleotides of SEQ ID NO:2 can contain a variant of itself, where in the SEQ ID NO:2 is the sum of a predefined set of nucleotide sequences.

5. Claims 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites "a transcription promoter operably linked to a selection from the group consisting of", which renders the scope of instant claim indefinite due an idiomatic error. Changing "a transcription promoter operably linked to a selection from the group consisting of" to -- a transcription promoter operably linked to a polynucleotide selected from the group consisting of – has been suggested.

6. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites "A cell comprising a selection form group consisting of", which renders the scope of instant claim indefinite due an idiomatic error. Changing "A cell

comprising a selection form group consisting" to -- A cell comprising a polynucleotide selected form group consisting – has been suggested.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Hiller et al (AN:H27701, 1995 and AN:H89576, 1995, see attached PTO SEQ search reports).

Claim 14 is drawn to a polynucleotide that hybridizes to either strand of a polynucleotides of SEQ ID NO:2 or SEQ ID NO:1.

Regarding a polynucleotide that hybridizes to the polynucleotides of SEQ ID NO:2. Hiller et al teaches a cDNA clone obtained from human Dystrophin gene (AN:H27701, 1995), which matches 100% to the nucleotide sequences of SEQ ID NO:2 at position 699 through 859. Considering the high level of sequence similarity, the cited art clearly anticipate a polynucleotide capable of hybridizing to the polynucleotide sequences of SEQ ID NO:2.

Regarding a polynucleotide that hybridizes to the polynucleotides of SEQ ID NO:1. Hiller et al teaches a cDNA sequence obtained from human Dystrophin gene (AN:H89576, 1995), which matches 100% to the nucleotide sequences of SEQ ID NO:1 at position 1 through 137. Considering the high level of sequence similarity, the cited art clearly anticipate a polynucleotide capable of hybridizing to the polynucleotide sequences of SEQ ID NO:1.

8. Claim 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hiller et al (AN:H89576, 1995, see attached PTO SEQ search report).

Claims 16-18 are drawn to a vector and host cells comprising the polynucleotides of SEQ ID NO:1 or a substantial equivalent thereof.

Hiller et al teaches a cDNA sequence obtained from human Dystrophin gene (AN:H89576, 1995), which matches 100% to the nucleotide sequences of SEQ ID NO:1 at position 1 through 137. The cited art further teaches the cloning of polynucleotide sequences of SEQ ID NO:1 in the pBluescript SK- expression vector and kanamycin resistance SOLR host cells (see Features Col.2, in the attaches sequence search report). Thus given the broadest reasonable interpretation the cited art clearly anticipate an expression vector and host cells which comprises the polynucleotides of SEQ ID NO:1 or a substantial functional equivalent thereof.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sumesh Kaushal
Examiner Art Unit 1636

SUMESH KAUSHAL
PATENT EXAMINER